


CERTIFICATE OF MAILING BY "EXPRESS MAIL"

I hereby certify that this correspondence is being deposited with the US Postal Services "Express Mail Post Office to Addressee" service under 37 CFR 1.10, Express Mail Label No. EL 967262881 US and addressed to MS Patent Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Date: November 20, 2003

By:   
Carol A. See

**PATENT**  
**Docket No. GC560-D1-C1**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of	)	
	)	
Volker Schellenberger <i>et al.</i>	)	
	)	Group Art Unit: Unassigned
Serial No.: Unassigned	)	
	)	Examiner: Unassigned
Filed: Herewith	)	
	)	
For: Directed Evolution of	)	
Microorganisms	)	

**Information Disclosure Statement**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Applicants submit herewith patents, publications or other information (listed on the attached Form PTO-1449 and attached thereto) of which they are aware, that they believe may be material to the examination of this application and in respect of which there may be a duty to disclose in accordance with 37 CFR §1.56.

This Information Disclosure Statement:

- (a) ☒ accompanies the new patent application submitted herewith. 37 CFR §1.97(a).
- (b) ☐ is filed within three months after the filing date of the application or within three months after the date of entry into the national stage of a PCT application as set forth in 37 CFR §1.491.
- (c) ☐ as far as is known to the undersigned, is filed before the mailing date of a first Office Action on the merits.
- (d) ☐ is filed after the first Office Action and more than three months after the

application filing date or PCT national stage date of entry filing but, as far as is known to the undersigned, prior to the mailing date of either a final rejection or a notice of allowance, whichever occurs first, and is accompanied by either the fee (\$180.00) set forth in 37 CFR §1.17(p) or a certification as specified in 37 CFR §1.97(e), as checked below. Authorization to charge Deposit Account No. 07-1048 in the amount of \$180.00 to cover the cost of this Information Disclosure Statement is provided in the Transmittal Letter submitted herewith in duplicate.

(e) ☐ is filed after the mailing date of either a final rejection or a notice of allowance, whichever occurred first, and is accompanied by authorization (in the Transmittal Letter submitted herewith in duplicate) to charge Deposit Account No. 07-1048 the fee (\$180.00) set forth in 37 CFR §1.17(l)(1) and a certification as specified in 37 CFR §1.97(e), as checked below. **This document is to be considered as a petition requesting consideration of the Supplemental Information Disclosure Statement.**

**[If either of boxes (d) or (e) is checked above, the following "certification" under 37 CFR §1.97(e) may need to be completed.]** The undersigned certifies that:

☐ Each item of information contained in the Information Disclosure Statement was cited in a communication mailed from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement.

☐ No item of information contained in this Information Disclosure Statement was cited in a communication mailed from a foreign patent office in a counterpart foreign application or, to the knowledge of the undersigned after making reasonable inquiry, was known to any individual designated in 37 CFR §1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

A copy of the items on Form PTO-1449 is supplied: PCT International Search Report for PCT/\_\_\_\_\_, filed \_\_\_\_\_ with attached patents and publications.

☐ each ☒ none ☐ only those listed below:

Those patent(s) or publication(s) which are marked with an asterisk (\*) on the attached Form PTO-1449 are not supplied because they were previously cited by or submitted to the Office in a prior application, Serial No. 09/314,847 filed May 19, 1999.

A concise explanation of relevance of the items listed on PTO-1449 is:

- ☒ not given
- ☐ given for each listed item
- ☐ given for only non-English language listed item(s)
- ☐ in the form of an English language copy of a Search Report from a foreign patent office, issued in a counterpart application, which refers to the relevant portions of the references.


The Examiner is reminded that a "concise explanation of the relevance" of the submitted prior art "may be nothing more than identification of the particular figure or paragraph of the patent or publication which has some relation to the claimed invention." MPEP §609.

While the information and references disclosed in this Information Disclosure Statement may be "material" pursuant to 37 CFR §1.56, it is not intended to constitute an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

In accordance with 37 CFR §1.97(b), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR §1.56(a) exists. It is submitted that the Information Disclosure Statement is in compliance with 37 CFR §1.98 and MPEP §609 and the Examiner is respectfully requested to consider the listed references.

Respectfully submitted,

Date: 19 November 2003

  
Kamrin T. MacKnight  
Registration No. 38,230

Genencor International, Inc.  
925 Page Mill Road  
Palo Alto, CA 94304-1013  
Tel: 650 846-5838  
Fax: 650 845-6504

**INFORMATION DISCLOSURE CITATION**

<b>Attorney Docket No.:</b> GC 560-D1-C1	<b>Serial No.:</b> Unassigned
<b>Applicant:</b> Schellenberger et al.	
<b>Filing Date:</b> Filed Herewith	<b>Group:</b> Unassigned
<b>Page</b> <u>1</u> <b>of</b> <u>3</u>	<b>Date of this Submission:</b> November 20, 2003

**US PATENT DOCUMENTS**

Examiner's	Document	Date	Name	Class	Sub-Class	Filing Date
Initial	Number	Date	Name	Class	Class	Date
	*5,716,785	02/10/98	Van Gelder et al.	435	6	
	*5,807,522	09/15/98	Brown et al.	422	50	

**FOREIGN PATENT DOCUMENTS**

Examiner's	Document	Date	Country	Class	Sub-Class	Translation
Initials	Number	Date	Country	Class	Class	Yes/No
	*WO/95/35505	12/28/95	PCT			
	*WO 98/21340	5/22/98	PCT			

**OTHER DOCUMENTS**

Examiner's	Document
Initials	Author, Title, Date, Pertinent Pages, etc.
	*Alexandre et al., "Relationship between ethanol tolerance, lipid composition and plasma membrane fluidity in <i>Saccharomyces cerevisiae</i> and <i>Kloeckera apiculata</i> ," <i>FEMS Microbiol. Lett.</i> , Vol. 124 (1), pp. 17-22 (1994)
	*Aono et al., "Preparation of Organic Solvent-tolerant Mutants from <i>Escherichia coli</i> K-12," <i>Agric. Biol. Chem.</i> , Vol. 55(7), pp.1935-1938 (1991)
	*Bennett et al., "Rapid evolution in response to high-temperature selection," <i>Nature</i> , Vol. 346, pp. 79-81 (1990)
	*Coia et al., "Use of Mutator Cells as a Means for Increasing Production Levels of a Recombinant Antibody Directed Against Hepatitis B," <i>Gene</i> , Vol. 201, pp. 203-209 (1997)
	*Cox et al., "Structure and coding properties of a dominant <i>Escherichia coli</i> mutator gene, mutD," <i>Proc Natl. Acad Sci USA</i> , Vol. 80, pp. 2295-2299 (1983)
	*Cruden et al., "Physiological Properties of a <i>Pseudomonas</i> Strain Which Grows with <i>p</i> -Xylene in a Two-Phase (Organic-Aqueous) Medium," <i>Appl. Environ. Microbiol.</i> , Vol. 58(9): pp. 2723-2729 (1992)
	*de Bont, "Solvent-tolerant bacteria in biocatalysis," <i>Trends in Biotechnology</i> , Vol. 16: pp. 493-499 (1998)
	*de Visser et al., "Diminishing Returns from Mutation Supply Rate in Asexual Populations," <i>Science</i> , Vol. 283, pp. 404-406 (1999)
	*Degenen et al., "Conditional Mutator Gene in <i>Escherichia coli</i> : Isolation, Mapping, and Effector Studies," <i>J. Bacteriol.</i> , Vol. 117, No. 2, pp.477-487, (1974)
	*DiFrancesco et al., "The Interaction of DNA Polymerase III and the Product of the <i>Escherichia coli</i> Mutator Gene, mutD*," <i>The Journal of Biological Chemistry</i> , Vol. 259 (9), pp. 5567-5573 (1984)
	*Dillon et al., "Spontaneous Mutation at the <i>mtr</i> Locus in <i>Neurospora</i> : The Molecular Spectrum in Wild-Type and a Mutator Strain," <i>Genetics</i> , Vol. 138(1), pp. 61-74 (1994)
	*Eigen et al., "The Origin of Genetic Information: Viruses as Models," <i>Gene</i> , Vol. 135, pp. 37-47 (1993)
	*Ginetti, " <i>Bacillus subtilis</i> <i>mutS</i> <i>mutL</i> operon: identification, nucleotide sequence and mutagenesis," <i>Microbiology</i> , Vol. 142 (Pt 8), pp. 2021-2029 (August 1996)
	*Greener et al., "Strategies In Molecular Biology," Vol. 7, pp.32-34, (1994)
	*Greener, et al., "An Efficient Random Mutagenesis Technique Using an <i>E. coli</i> Mutator Strain," <i>Molecular Biotechnology</i> (1997) Vol. 7. pp. 189-195 (XP-000974365)

<b>Examiner</b>	<b>Date Considered</b>

Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

PTO-1449

**INFORMATION DISCLOSURE CITATION**

<b>Attorney Docket No.:</b> GC 560-D1-C1	<b>Serial No.:</b> Unassigned
<b>Applicant:</b> Schellenberger et al.	
<b>Filing Date:</b> Filed Herewith	<b>Group:</b> Unassigned
<b>Page</b> <u>2</u> <b>of</b> <u>3</u>	<b>Date of this Submission:</b> November 20, 2003

**US PATENT DOCUMENTS**

Examiner's	Document				Sub-	Filing
Initial	Number	Date	Name	Class	Class	Date

**OTHER DOCUMENTS**

Examiner's	
Initials	Author, Title, Date, Pertinent Pages, etc.
	*Hall et al., "Evolutionary Potential of the <i>ebgA</i> Gene," <i>Mol. Biol. Evol.</i> , Vol. 12, No. 3, pp. 514-517 (1995)
	*Harder et al., "A Review Microbial Selection in Continuous Culture," Vol. 43, pp. 1-24 (1977)
	*Heery et al., "Curing of a plasmid from <i>E.coli</i> using high-voltage electroporation," <i>Nucl. Acids. Res., E. coli</i> , Vol. 17, pp. 10131 (1989)
	*Horiuchi et.al, "A New Conditional Lethal Mutator ( <i>dnaQ49</i> ) in <i>Escherichia coli</i> K12," <i>Mol. Gen. Genetics</i> , Vol. 163, pp. 277-283 (1978)
	*Inoue, "A <i>Pseudomonas</i> thrives in high concentrations of toluene," <i>Nature</i> , Vol. 338, pp. 264-266 (1989)
	*Irving et al., "Affinity Maturation of Recombinant Antibodies Using <i>E. coli</i> Mutator Cells," <i>Immunotechnology</i> , Vol. 2, pp. 127-143 (1996)
	*Isken et.al, "Bacteria tolerant to organic solvents," <i>Extremophiles</i> , Vol. 2 (3), pp. 229-238 (1998)
	*Kieboom et al., "Active Efflux of Organic Solvents by <i>Pseudomonas putida</i> S12 Is Induced by Solvents," <i>J. of Bacteriology</i> , Vol.180(24), pp. 6769-6772 (1998)
	*MacDonald et al., "Microsatellite Instability and Loss of Heterozygosity at DNA Mismatch Repair Gene Loci occurs During Hepatic Carcinogenesis," <i>Hepatology</i> , Vol. 28(1), pp. 90-97 (1998)
	*Maki et al., "Structure and expression of the <i>dnaQ</i> mutator and the RNase H genes of <i>Escherichia coli</i> : Overlap of the promoter regions," <i>Proc. Natl. Acad. Sci., U.S.A.</i> Vol. 80, pp. 7137-7141 (1983)
	*Mao et al., "Proliferation of Mutators in A Cell Population," <i>Journal of Bacteriology</i> , V. 179 (2), pp. 417-422 (1997)
	*Maruyama et al., "A Dominant ( <i>mutD5</i> ) and a Recessive ( <i>dnaQ49</i> ) Mutator of <i>Escherichia coli</i> ," <i>Journal of Molecular Biology</i> , Vol. 167, pp. 757-771 (1983)
	*Miller, J.H., "A Short Course in Bacterial Genetics," <i>Cold Spring Harbor Lab Press</i> , pp. 110-113 (1992)
	*Miller, "Experiments in Molecular Genetics," <i>Episomes, E.Coli, Acridine Orange Molecular Genetics</i> , p. 140 (1972)
	*Naki, et al., "Selection of a subtilisin-hyperproducing <i>Bacillus</i> in a highly structured environment," <i>Appl. Microbiol. Biotechnol.</i> (1998) 49: pp. 290-294 (XP-000972404)
	*Pham et.al, "The Base Substitution and Frameshift Fidelity of <i>Escherichia coli</i> DNA Polymerase III Holoenzyme in Vitro*," <i>J. of Biol. Chem.</i> , Vol. 273(36) , pp. 23575-23584 (1998)
	*Pinkart et.al, "Phospholipid Biosynthesis and Solvent Tolerance in <i>Pseudomonas putida</i> Strains," <i>J. Bacteriol</i> , Vol.179(13), pp. 4219-4226 (1997)
	*Priebe et al., "Nucleotide Sequence of the <i>hexA</i> Gene for DNA Mismatch Repair in <i>Streptococcus pneumoniae</i> and Homology of <i>hexA</i> to <i>mutS</i> of <i>Escherichia coli</i> and <i>Salmonella typhimurium</i> ," <i>J. Bacteriol</i> , Vol. 170(1), pp. 190-196 (1988)
	*Prudhomme et al., "Mismatch Repair Genes of <i>Streptococcus pneumoniae</i> : HexA Confers a Mutator Phenotype in <i>Escherichia coli</i> by Negative Complementation," <i>J. Bacteriol.</i> ; Vol. 173(22), (1991)
	*Prudhomme et al., "Nucleotide Sequence of the <i>Streptococcus pneumoniae</i> <i>hexB</i> Mismatch Repair Gene: Homology of HexB to MutL of <i>Salmonella typhimurium</i> and to PMS1 of <i>Saccharomyces cerevisiae</i> ," <i>J. Bacteriology</i> , Vol. 171 (10), pp. 5332-8 (1989)

<b>Examiner</b>	<b>Date Considered</b>

Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

PTO-1449

**INFORMATION DISCLOSURE CITATION**

<b>Attorney Docket No.:</b> GC 560-D1-C1	<b>Serial No.:</b> Unassigned
<b>Applicant:</b> Schellenberger et al.	
<b>Filing Date:</b> Filed Herewith	<b>Group:</b> Unassigned
<b>Page</b> <u>  3  </u> <b>of</b> <u>  3  </u>	<b>Date of this Submission:</b> November 20, 2003

**US PATENT DOCUMENTS**

Examiner's	Document				Sub-	Filing
Initial	Number	Date	Name	Class	Class	Date

**FOREIGN PATENT DOCUMENTS**

Examiner's	Document				Sub-	Translation
Initials	Number	Date	Country	Class	Class	Yes/No

**OTHER DOCUMENTS**

Examiner's	
Initials	Author, Title, Date, Pertinent Pages, etc.
	*Ramos, et al., "Mechanisms for Solvent Tolerance in Bacteria," <i>J. Biol. Chem.</i> , Vol. 272(7), pp. 3887-3890 (1997)
	*Roa, et al., "Changing the substrate specificity of penicillin G acylase from <i>Kluyvera citrophila</i> through selective pressure," <i>Biochem. J.</i> (1994) 303, pp. 8*69-876 (XP-000972422)
	*Schaaper, "An <i>Escherichia coli</i> dnaE Mutation with Suppressor Activity toward Mutator mutD5," <i>Journal of Bacteriology</i> , Vol. 174(6), pp. 1974-1982 (1992)
	*Schaaper, "Mechanisms of mutagenesis in the <i>Escherichia coli</i> mutator mutD5: Role of DNA mismatch repair," <i>PNAS</i> , Vol. 85, pp. 8126-8130 (1988)
	*Schellenberger, "Directed evolution of subtilisin for improved surface proteolysis," (1998) BTEC 73, Vol. 216, No. 1-3 (XP000972454)
	*Sniegowski et.al, "Evolution of high mutation rates in experimental populations of <i>E. coli</i> ," <i>Nature</i> , Vol. 387, pp. 703-705 (1997)
	*Snyder et.al, "Molecular genetics of bacteria," <i>American Society for Microbiology</i> , chap. 3: pp. 85-89 (1997)
	*Taddei et.al, "Role of mutator alleles in adaptive evolution," <i>Nature</i> , Vol. 387, pp. 700-702 (1997)
	*Taft-Benz et al., "Mutational analysis of the 3'→5'proofreading exonuclease of <i>Escherichia coli</i> DNA polymerase III," <i>Nucl. Acids Res.</i> , Vol. 26(17), pp. 4005-4011 (1998)
	*Takano et al., "Structure and function of <i>dnaQ</i> and <i>mutD</i> mutators of <i>Escherichia coli</i> ," <i>Mol. Gen. Genet.</i> , Vol. 205(1), pp. 9-13 (1986)
	*Trobner et.al, "Selection against hypermutability in <i>Escherichia coli</i> during long term evolution," <i>Mol. Gen Genet</i> , Vol. 198, pp. 177-178 (1984)
	*Weber et al., "Adaptation of <i>pseudomonas putida</i> S12 to High Concentrations of Styrene and Other Organic Solvents," <i>Appl. Environ. Microbiol.</i> , Vol. 59(10), pp. 3502-3504 (1993)
	*Yamagishi, et al., "Mutational analysis of structure – activity relationships in human tumor necrosis factor-alpha," <i>Protein Engineering</i> , Vol. 3, No. 8, pp. 713-719 (1990) (XP-000971051)
	*Yomano, "Isolation and characterization of ethanol-tolerant mutants of <i>Escherichia coli</i> KO11 for fuel ethanol production," <i>J. Ind. Microbiol. Biotechnol.</i> , Vol. 20(2): pp. 132-138 (1998)
	*Copy of International Search Report for PCT/US00/13337

<b>Examiner</b>	<b>Date Considered</b>

<b>Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	<b>PTO-1449</b>